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Unlocking the potential of high-volume SIMS data with molecular formula prediction

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A significant advantage of secondary ion mass spectrometry (SIMS) is the capability to map multiple classes of molecules simultaneously in an untargeted label-free manner. This is especially so for OrbiSIMS data where reduced fragmentation enabled by the GCIB primary beam and high mass resolving power of the Orbitrap™ analyser allow chemical characterisation of biological samples[1]. However, the complex character of the data and the fact that the spectra contain both intact molecular ions and fragmented ions, complicates the untargeted investigation of biological samples and this advantage of the OrbiSIMS cannot be fully utilised without considerable investment in data analysis strategies.

We use the concept of chemical filtering via molecular formula prediction (MFP) and the level of molecule unsaturation (double bond equivalents) to filter OrbiSIMS assignments[2]. We integrate the LIPIDMAPS® database and generate a protein fragment database to facilitate chemical filtering and assignment of these molecules. This approach is now a routine aspect of OrbiSIMS data analysis and has been successfully applied to several biological samples, assigning salts, lipids and protein fragments in human serum[2], mapping different lipid classes throughout human skin[3] and tracking lipids, polysaccharides, glycolipids and protein fragments in a bacterial biofilm[4].

This talk will describe the interpretation of complex biological datasets enabled by the molecular formula prediction approach. Particularly, it focuses on the chemical filtering and assignment of poorly ionisable molecules (e.g. protein fragments), which are likely to be missed in statistical analysis. In addition to filtering protein fragments, this method enables rapid assignment and classification of protein ions. This improvement can help predict which fragments will be seen in the OrbiSIMS spectrum and identify proteins in an analogous way as the proteomics community has developed for liquid chromatography MS.

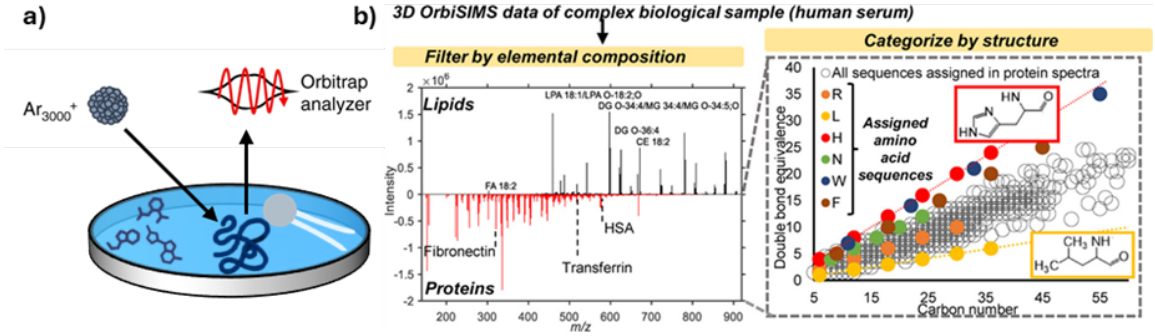

Figure 1 Automatic assignment of lipid and protein fragments in human serum. **a)** Schematic of the experiment **b)** Molecular formula prediction

References:
1. Passarelli, M.K. *et al. Nat. Methods* (2017).
2. Edney, M.K. *et al. Anal. Chem.* (2022).
3. Starr N.J. *et al. PNAS* (2022).
4. Kotowska A.M. *et al. Analytical Chemistry* (2023)